

## **REMARKS**

### **1. Status of the Claims**

Claims 9-11 have been cancelled, several claims have been amended, and claims 20-22 have been added to the application.

Independent claims 2, 4 and 18 have been amended to define that the hyaluronic acid derivative is either a benzyl ester of hyaluronic acid or an auto-crosslinked ester of hyaluronic acid.

Claims 3 and 4 have been amended to define the percentage of esterification for the benzyl ester. These amendments are supported by the Specification at, for example, page 8, lines 28-29.

Claims 8, 16 and 21 define that the auto-crosslinking is in an amount of 5% of the carboxy groups. These amendments are supported by the Specification at, for example, page 11, line 4.

New claim 22 specifically defines that the benzyl ester is a 75% benzyl ester. This claim is supported by the Specification at, for example, Example 1 on pages 27-28 of the application.

As a result, claims 3-8 and 12-22 are presented for examination.

### **2. Rejection of the Claims Under 35 USC § 112**

Claims 3-19 have been rejected under 35 USC § 112, second paragraph. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

As noted above, the claims have been amended to refer to either a benzyl ester of hyaluronic acid or an auto-crosslinked ester of hyaluronic acid. The nature of these two products is well described in the application. For example, page 7, line 2 through the bottom of page 9 describes various types of esters of hyaluronic acid with alcohols, and the application then describes the preparation of such esters. Example 1 in the application is specifically directed to experiments utilizing the benzyl ester of hyaluronic acid, the preparation of which is described in EP 216453B1 cited at page 6, lines 12 and 22 of the application. The auto-crosslinked esters of

hyaluronic acid are described in the application beginning at the top of page 11, with further description of the preparation process described in EP 0341745B1 cited at page 6, line 25 of the application. Applicants, therefore, submit that the claims do indeed particularly point out and distinctly claim the present invention as required by the second paragraph of section 112.

Accordingly, reconsideration and withdrawal of the rejection are requested.

### **3. Rejection of the Claims Under 35 USC § 102**

Claims 3-8, 12 and 14-18 have been rejected under 35 USC § 102(b) over *Davidson et al.* This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

*Davidson et al.* only describe studies relating to the use of hyaluronic acid or an ethyl ester of hyaluronic acid. The present claims, as amended, are directed to the use of either a benzyl ester or an auto-crosslinked ester of hyaluronic acid. Since the products used and the methods are different, *Davidson* does not anticipate the present invention.

Therefore, reconsideration and withdrawal of the rejection are requested.

### **4. Rejection of the Claims Under 35 USC § 103**

Claim 3-19 have been rejected under 35 USC § 103(a) over *Davidson et al.* in view of *Della Velle et al.* (U.S. Patent 5,676,964) or in view of *Della Velle* (U.S. Patent 4,851,521). These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

As noted above, the claims as amended are directed to a method utilizing either a benzyl ester of hyaluronic acid or an auto-crosslinked ester of hyaluronic acid. *Davidson et al.*, on the other hand, is limited to use of either hyaluronic acid or an ethyl ester of hyaluronic acid. Thus, *Davidson et al.* does not teach or suggest the specific hyaluronic acid derivatives recited in the present claims.

The two *Della Velle et al.* patents show that the benzyl ester derivative and the auto-crosslinked ester derivative of hyaluronic acid were *per se* known in the art. However, those two patents

describe various types of hyaluronic acid derivatives, and the use of specifically a benzyl ester or an auto-crosslinked ester in the method of the present invention would not be obvious because of the unexpected results achieved by means of the present invention.

In support of the non-obvious and unexpected results achieved by means of the present invention, enclosed herewith is a Declaration Under 37 CFR 1.132 by Anna Maria Zanellato. The Zanellato Declaration reports on comparative test results with the use of the benzyl ester and auto-crosslinked hyaluronic acid derivatives recited in the present claims as compared to products described in *Davidson et al.*, specifically the ethyl ester of hyaluronic acid, an alginate vehicle and hyaluronic acid. Two different studies were conducted with the products, the first study being directed to a wound healing model and the second study being directed to a model for investigating cutaneous scarring following treatment of a wound. As shown by the test results reported in Attachment 2 of the Zanellato Declaration, treatment with the benzyl ester or the auto-crosslinked ester product resulted in unexpectedly reduced scarring as compared to treatment with either the ethyl ester as described in *Davidson* or with hyaluronic acid. The results are particularly summarized in the graph of Attachment 2 of the Declaration, from which it can be seen that as early as day 14 the scarred areas of the treatment groups (i.e. those treated with the auto-crosslinked or the benzyl ester) were 40% less extensive than the control untreated areas; whereas, the wounds treated with either hyalastine (i.e. hyaluronic acid) or with the ethyl ester were more extensive than the control untreated areas. This means that scarring in the groups treated with either hyalastine or with the ethyl esters was actually increased as compared to control untreated animals; whereas, scarring was reduced by about 40% for those groups treated with either the benzyl ester or the auto-crosslinked ester derivative.

Applicants submit that these test results evidence the completely unexpected and superior nature of the present invention as compared to the prior art when tested in direct side-by-side experiments. One skilled in the art simply could not have expected the products used in the present invention to reduce scarring by as much as 40% when the products described in the prior art actually increase scarring as compared to control.

The unexpected and surprising nature of the results achieved by the present invention are further attested to in the Zanellato Declaration.

In accordance with the above, reconsideration of all the rejections, and early allowance of the claims are requested.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of \$490.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

If the Examiner has any questions concerning this application, the Examiner is requested to contact Leonard R. Svensson, Reg. No. 30,330 at the telephone number of (858) 792-8855. Facsimile communications may be sent to Leonard R. Svensson at the facsimile number of (858) 792-3785.

Dated: February 3, 2009

Respectfully submitted,

By 

Leonard R. Svensson

Registration No.: 30,330

BIRCH, STEWART, KOLASCH & BIRCH, LLP

12770 High Bluff Drive

Suite 260

San Diego, California 92130

(858) 792-8855

Attorney for Applicant